

## REMARKS

The above amendments and these remarks are responsive to the final Office action dated January 27, 2005, and support the accompanying Request for Continued Examination as a submission under 37 C.F.R. § 1.114. Claims 1-4, 7-10, 12, 17, and 47-60 are pending in the application. In the Office action, the Examiner rejected all of the pending claims:

- Claims 7, 8, 56, and 57 were rejected under 35 U.S.C. § 112, second paragraph
- Claims 1-3, 8, 9, 12, 17, and 60 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,287,774 to Nikiforov ("Nikiforov")
- Claims 4, 7, 10, and 47-59 were rejected under 35 U.S.C. § 103(a) over the following reference(s):
  - Nikiforov alone (claim 4)
  - Nikiforov in view of U.S. Patent No. 6,022,708 to de Sauvage et al. ("de Sauvage") (claim 7)
  - Nikiforov in view of U.S. Patent No. 5,424,190 to Fuller ("Fuller") (claims 47-49)
  - Nikiforov in view of U.S. Patent No. 4,421,735 to Haber et al. ("Haber") (claims 10, 50-52, 54, 55, 57, and 59)
  - Nikiforov in view of Haber and de Sauvage (claim 56)
  - Nikiforov in view of Haber and Fuller (claims 53 and 58)

Applicants traverse these rejections. Applicants contend that the rejected claims are not indefinite, anticipated, or obvious. Nevertheless, to reduce the number of issues under consideration, and to expedite the issuance of a patent, applicants have canceled claims 1-4, 7-10, 12, 17, 47-49, and 60, without prejudice; have amended claims 51, 52, 56, 57, and 59; and have added new claims 61-66. Applicants reserve the right to pursue any of the canceled claims at a later time. Moreover, applicants have presented arguments showing that the claimed invention is neither taught nor suggested by the

references of record. Accordingly, applicants respectfully request reconsideration of the rejected claims and prompt issuance of a Notice of Allowability.

**I. Request for Continued Examination**

Applicants are submitting herewith a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114. This Request complies with the requirements of 37 C.F.R. § 1.114. In particular:

- (i) Prosecution in the application is closed, since the last Office action was a final Office action under 37 C.F.R. § 1.113.
- (ii) The Request is accompanied by a submission as set forth at 37 C.F.R. § 1.114(c), specifically, the amendments, remarks, and arguments set forth herein.
- (iii) The Request is accompanied by the fee set forth at 37 C.F.R. § 1.17(e).

Accordingly, applicants respectfully request grant of their Request for Continued Examination.

**II. Rejections under 35 U.S.C. § 112**

The Examiner rejected claims 7, 8, 56, and 57 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully disagree, and suggest that one of ordinary skill in the art, provided with the guidance of the specification, would well understand the claimed subject matter definitely and particularly. However, in the interest of facilitating prosecution of the application, applicants have canceled claims 7 and 8, and amended claims 56 and 57.

In rejecting claim 56, the Examiner stated that there is no antecedent basis for the phrase "the formation of unlabelled phosphorylated protein." Applicants have addressed this rejection by amending claim 56 as follows:

56. (Currently Amended) The method of claim 55, wherein there is at least one phosphate group on the luminescent peptide, further comprising catalyzing ~~[[the]]~~ formation of unlabelled phosphorylated protein in the reaction mixture to competitively bind to the binding partner.

In particular, applicants have deleted “the” from “the formation....” Applicants believe amended claim 56 meets the requirements of 35 U.S.C. § 112, second paragraph.

In rejecting claim 57, the Examiner stated that claim 57 is vague because it is not clear as to the function of the phosphorylated protein. Applicants have addressed this rejection by amending claim 57 as follows:

57. (Currently Amended) The method of claim 55, wherein the binding partner is capable of binding ~~[[binds]]~~ specifically to a phosphorylated protein substantially without regard to the particular amino acid sequence of the protein.

Accordingly, amended claim 57 clarifies that a property of the binding partner is being recited, namely, that the binding partner is capable of binding specifically to a phosphorylated protein. However, the Examiner also stated that it is “not clear as to how the binding partner can bind specifically to the protein without regard to the amino acid sequence of the protein.” Applicants suggest that the binding partner is capable of binding specifically to a phosphorylated form of the protein, relative to a nonphosphorylated form of the protein, without regard to the particular amino acid sequence of the protein. The Examiner asked: “Any binding partner will work?” Applicants do not entirely understand this question but believe that the question is answered by the amendment to claim 57 and the foregoing discussion about the capability of the binding partner. In any case, applicants believe amended claim 57 meets the requirements of 35 U.S.C. § 112, second paragraph.

### **III. Rejections under 35 U.S.C. § 102**

The Examiner rejected claims 1-3, 8, 9, 12, 17, and 60 in the Office action under 35 U.S.C. § 102(e) as being anticipated by Nikiforov. Applicants traverse these rejections. However, to reduce the number of issues under consideration, and to expedite issuance of a patent, applicants have canceled each of these claims, rendering the corresponding rejections moot.

### **IV. Rejections under 35 U.S.C. § 103**

#### **A. Claims 4, 7, 10, and 47-49**

The Examiner rejected claims 4, 7, 10, and 47-49 in the Office action under 35 U.S.C. § 103(a) over Nikiforov alone or in combination with de Sauvage, Haber, or Fuller. Applicants traverse these rejections. However, to reduce the number of issues under consideration, and to expedite issuance of a patent, applicants have canceled each of these claims, rendering the corresponding rejections moot.

#### **B. Claims 50-59**

Claim 50 is directed to a method and recites:

50. (Previously Presented) A method of detecting addition or removal of a phosphate group to or from a substrate, comprising:

contacting a luminescent peptide with a binding partner that binds specifically to the peptide only if the peptide is phosphorylated, wherein the binding partner includes gallium involved in binding between the binding partner and the peptide, and wherein the peptide is a substrate for an enzyme that catalyzes addition or cleavage of a phosphate group to or from the peptide; and

measuring luminescence polarization from the luminescent peptide, wherein the amount of measured luminescence polarization can be related to the extent of binding between the luminescent peptide and the binding partner.

The Examiner rejected claim 50 as being obvious over Nikiforov in view of Haber.

Applicants traverse this rejection.

The references cited by the Examiner must satisfy several basic criteria to establish the *prima facie* obviousness of rejected claims. For example, the cited

references must teach or suggest every element of the claims. In addition, there must be some suggestion or motivation within the cited references to modify the reference teachings to obtain the claimed invention. Applicants assert that the Examiner has failed to establish the *prima facie* obviousness of claim 50, at least because (1) the cited references do not teach or suggest every element of claim 50, and (2) there is no suggestion or motivation to combine the reference teachings.

1. *Nikiforov and Haber Do Not Teach or Suggest Every Element*

Applicants assert that Nikiforov and Haber, alone or in combination, do not teach or suggest every element of claim 50. For example, neither Nikiforov nor Haber teaches or suggests a binding partner that includes gallium involved in binding between the binding partner and a luminescent peptide, as recited by claim 50.

Nikiforov relates to assay systems that purport to use polyions to affect the fluorescence polarization measured from a reaction mixture. For example, Nikiforov discloses a kinase assay using a fluorescently labeled, phosphorylatable substrate contacted with a kinase enzyme and with a polycation (col. 13, lines 18-26). The polycation is intended to bind preferentially to the phosphorylated form of the substrate, based on a charge difference, to selectively increase its size and decrease its rotational diffusion rate (col. 13, lines 29-31), thereby increasing the fluorescence polarization value (col. 13, lines 12-16). Nikiforov also discloses a set of multivalent metal cations, namely,  $\text{Fe}^{3+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Ni}^{2+}$ , and  $\text{Zn}^{2+}$ , that it asserts can be associated with a large molecule, such as a protein, to provide a suitable polyionic component for use in the assays (col. 13, lines 32-36). However, among other differences, Nikiforov does not teach or suggest a "binding partner [that] includes gallium involved in binding between the binding partner and the [luminescent] peptide," as recited by claim 50. In the Office

action, the Examiner reached the same conclusion about the deficiency of Nikiforov in teaching gallium (Office action, dated January 27, 2005, pg. 8, lines 1-2).

Haber relates to formation of radiolabeled proteins for diagnostic use. The proteins are covalently coupled to a chelating agent, which in turn binds a radioactive molecule (col. 1, lines 48-50). Haber discloses radioactive gallium-68 and gallium-67 as multivalent cationic radioisotopes that can be used as the radioactive molecule coupled to a protein (col. 2, lines 21-25).

However, Haber does not teach or suggest “gallium involved in binding between the binding partner and the [luminescent] peptide,” as recited by claim 50. More specifically, Haber discloses various proteins that are involved in binding in diagnostic assays. For example, Haber discloses “antibodies, antigens, [and] antibody fragments” (col. 1, lines 44-47), such as anti-alpha feto protein, anti-CEA, anti-myosin, and fibrinogen (col. 1, lines 64-68; col. 4, lines 45-49)), which have an intrinsic binding activity in diagnostic assays. The proteins are attached to radioactive molecules (such as radioactive gallium) that are intended to radiolabel the proteins. The radioactive molecules reportedly allow the proteins to be used for scintigraphy in vivo or radioimmunoassay in vitro (col. 3, lines 15-19), without deactivation of the proteins’ biological (e.g., binding) activities (col. 1, lines 45-47). Accordingly, the radioactive gallium disclosed by Haber is intended to have no effect on the proteins’ ability to bind in diagnostic assays. The radioactive gallium thus is not involved in binding by the radiolabeled proteins during assays, rather than being “involved in binding,” as recited by claim 50.

## 2. No Suggestion or Motivation to Combine References

Applicants assert that there is no suggestion or motivation to combine the teachings of Nikiforov with those of Haber to achieve the claimed invention. Nikiforov involves assays that measure fluorescence polarization of a fluorescent peptide tagged with a fluorescent label. In contrast, Haber involves assays that measure radioactive decay of a radiolabeled protein tagged with a radioactive label (such as radioactive gallium). One of skill in the art would have considered fluorescence assays and radiolabeling assays to be distinct and somewhat mutually exclusive. (See, e.g., the final paragraph of the Background in the present application.) In particular, one of skill in the art would have considered the fluorescent label of Nikiforov and the radioactive gallium of Haber to be serving analogous labeling functions in providing a measurable signal. Accordingly, it would not have been obvious, at the time of the invention, to replace the cations disclosed by Nikiforov with radioactive gallium, because the cations of Nikiforov are providing a different function than the radioactive gallium of Haber. In particular, the cations of Nikiforov are stated to have a role in binding fluorescent peptide, whereas the radioactive gallium of Haber is disclosed to have a role in labeling, rather than binding, during diagnostic assays. Accordingly, one of skill in the art would not have been motivated to replace the cations of Nikiforov with the radioactive gallium of Haber.

## 3. Summary

The Examiner has failed to establish the *prima facie* obviousness of claim 50, at least because (1) the cited references do not teach or suggest every element of the claim, and (2) because there is no suggestion or motivation in the cited references to combine the reference teachings. Claim 50 thus should be allowed. Claims 51-59,

which depend from allowable claim 50, also should be allowed for at least the same reasons as claim 50.

**V. Amendments / New Claims**

Applicants have amended claims 51, 52, and 59 to address formatting matters and/or correct typographical errors (in addition to the amendments of claims 56 and 57 discussed above, in Section II). In particular, claim 59 has been amended to depend from claim 55 instead of claim 50.

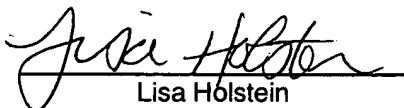
Applicants also have added new claims 61-66 to more particularly point out and distinctly claim aspects of the invention. These claims are supported fully by the application. Furthermore, these claims should be allowed, at least for depending from allowable claim 50.

**VI. Conclusion**

Applicants believe that this communication is fully responsive to the Office Action, and that the claims are currently in condition for allowance. However, if there are any remaining matters, or if it would otherwise advance prosecution of the application, the Examiner is encouraged to call the undersigned attorney at (503) 224-6655.

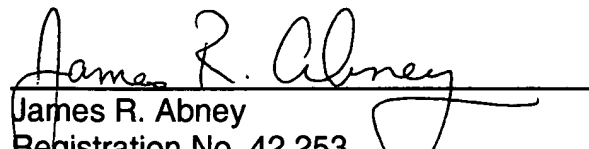
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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on July 20, 2005.

  
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